

CLAIMS

What we claim is:

1. A method for generating in a host a virus neutralizing level of antibodies to a primary HIV isolate, comprising:

at least one administration of a priming antigen to the host, wherein the priming antigen comprises a DNA molecule encoding an envelope glycoprotein of a primary isolate of HIV-1,

resting the host for at least one specific resting period to provide for clonal expansion of an HIV antigen specific population of precursor B-cells therein to provide a primed host, and

at least one administration of a boosting antigen to the primed host to provide said neutralizing levels of antibodies, wherein the boosting antigen is selected from the group consisting of a non-infectious, non-replicating, immunogenic HIV-like particle having at least the envelope glycoprotein of a primary isolate of HIV-1 and an attenuated viral vector expressing at least an envelope glycoprotein of a primary isolate of HIV-1.

2. The method of claim 1 wherein said primary isolate is Bx08.
3. The method of claim 2 wherein said DNA molecule is contained in a plasmid vector under the control of a heterologous promoter for expression of the envelope glycoprotein in the host.
4. The method of claim 3 wherein the promoter is the cytomegalovirus promoter.
5. The method of claim 4 wherein the vector has the identifying characteristics of pCMV3Bx08 shown in Figure 2.
6. The method of claim 1 wherein the at least one administration of a priming antigen is at least two administrations of the priming antigen.
7. The method of claim 6 wherein the at least one specific resting period is effected after each priming administration.
8. The method of claim 1 wherein the at least one specific resting period is between about 2 months to about 12 months.
9. The method of claim 1 wherein said non-infectious, non-replicating, immunogenic HIV-like particle comprises an assembly of:
  - (i) an *env* gene product,

(ii) a *pol* gene product, and

(iii) a *gag* gene product,

said particle being encoded by a modified HIV genome deficient in long terminal repeats (LTRs) and containing *gag*, *pol* and *env* in their natural genomic arrangement.

10. The method of claim 9 wherein the *env* gene is that from primary isolate BX08.

11. The method of claim 1 wherein said non-infectious, non-replicating, immunogenic HIV-like particle is administered in conjunction with an adjuvant.

12. The method of claim 11 wherein the adjuvant is QS21.

13. The method of claim 1 wherein said attenuated viral vector is an attenuated avipoxvirus

14. The method of claim 13 wherein the attenuated viral vector contains a modified HIV-genome deficient in long terminal repeats, wherein at least the *env* gene is that from primary isolate BX08.

15. The method of claim 14 wherein the attenuated avipoxvirus vector is the attenuated canary poxvirus ALVAC.

16. The method of claim 15 wherein the attenuated canary poxvirus vector has the identifying characteristics of vCP1579.

17. The method of claim 1 wherein the at least one administration of a boosting antigen is at least two administrations of a boosting antigen.

18. A vector, comprising a DNA sequence encoding an envelope glycoprotein of a primary isolate of HIV-1 under the control of a heterologous promoter for expression of the envelope glycoprotein in a host organism.

19. The vector of claim 18 wherein the vector is a plasmid vector.

20. The vector of claim 18 wherein said primary HIV-1 isolate is Bx08.

21. The vector of claim 20 wherein the promoter is the cytomegalovirus promoter.

22. The vector of claim 21 which has the identifying characteristics of pCMV3Bx08 shown in Figure 2.

23. The vector of claim 18 wherein the vector is an attenuated viral vector.

24. The vector of claim 23 wherein the attenuated viral vector is a attenuated avipoxvirus vector.

25. The vector of claim 24 wherein the attenuated avipoxvirus vector is the attenuated canary poxvirus vector ALVAC.

26. The vector of claim 25 wherein the attenuated viral vector has the identifying characteristics of vCP1579 shown in Figure 4.

27. A vector, comprising a modified HIV genome deficient in long terminal repeats and a heterologous promoter operatively connected to said genome for expression of said HIV genome in mammalian cells to produce non-infectious, non-replicating and immunogenic HIV-like particles, wherein at least the *env* gene is that from a primary isolate of HIV-1.

28. The vector of claim 27 wherein the vector is a plasmid vector.

29. The vector of claim 28 wherein the primary HIV-1 isolate is BX08.

30. The vector of claim 29 wherein the promoter is type IIA metallothionein promoter.

31. The vector of claim 30 which has the identifying characteristics of p133B1 shown in Figure 3.